

In the Claims

Please amend claims 1, 7, 10, 11, 20, 21, 24, 34, 43, 56, and 86, and add new claims 87-102, as noted below.

1. (currently amended) A method for treating a subject having a B-cell malignancy, wherein cells of the malignancy upregulate expression of an antigen in response to immunostimulatory CpG oligonucleotide, the method comprising:

administering to ~~a subject~~ the subject having a B-cell malignancy (a) an immunostimulatory CpG oligonucleotide between 6 and 100 nucleotides long comprising a backbone modification and at least the formula 5' X₁X₂CGX₃X₄ 3', wherein C is unmethylated and wherein X₁, X₂, X₃, and X₄ are nucleotides, in an effective amount to upregulate ~~CD20~~ expression of the antigen by the cells ~~and (b); and~~

administering to the subject an anti-CD20 antibody, wherein the administering the CpG oligonucleotide and the anti-CD20 antibody results in treating the B-cell malignancy specific for the upregulated antigen, in an effective amount to treat the subject.

2-6. (canceled)

7. (currently amended) The method of claim 1, wherein the B-cell malignancy is a B-cell lymphoma associated with low levels of CD20 expression, the antigen is CD20, and the antibody is an anti-CD20 antibody.

8. (original) The method of claim 7, wherein the B-cell lymphoma is B-cell chronic lymphocytic leukemia (B-CLL).

9. (original) The method of claim 7, wherein the B-cell lymphoma is a marginal zone lymphoma.

10. (currently amended) The method of ~~claim 1~~ claim 7, wherein the anti-CD20 antibody is C2B8.

11. (currently amended) The method of ~~claim 1~~ claim 7, wherein the anti-CD20 antibody is Rituximab.

12-13. (canceled)

14. (previously presented) The method of claim 1, wherein the modified backbone is a phosphate backbone modification.

15. (previously presented) The method of claim 1, wherein the modified backbone is an amino acid backbone.

16. (canceled)

17. (previously presented) The method of claim 1, wherein the immunostimulatory CpG oligonucleotide is 8 to 40 nucleotides in length.

18. (previously presented) The method of claim 1, wherein the immunostimulatory CpG oligonucleotide is isolated.

19. (previously presented) The method of claim 1, wherein the immunostimulatory CpG oligonucleotide is a synthetic nucleic acid.

20. (currently amended) The method of ~~claim 1~~ claim 7, wherein the immunostimulatory CpG oligonucleotide and the anti-CD20 antibody are administered together.

21. (currently amended) The method of ~~claim 1~~ claim 7, wherein the immunostimulatory CpG oligonucleotide and the anti-CD20 antibody are administered separately.

22-23. (canceled)

24. (currently amended) A method for treating ~~B-cell malignancy~~ a subject having a marginal zone lymphoma or B-cell chronic lymphocytic leukemia, wherein cells of the lymphoma or leukemia upregulate expression of an antigen in response to immunostimulatory CpG oligonucleotide, the method comprising:

administering to ~~a subject having a B-cell malignancy, wherein said B-cell malignancy is a marginal zone lymphoma or B-cell chronic lymphocytic leukemia (B-CLL)~~, the subject an immunostimulatory CpG oligonucleotide between 6 and 100 nucleotides long comprising a backbone modification and at least the formula 5' X₁X₂CGX₃X₄ 3', wherein C is unmethylated and wherein X₁, X₂, X₃, and X₄ are nucleotides, in an effective amount to ~~induce~~ upregulate expression of ~~a surface antigen on a cancer cell surface, wherein said surface antigen is chosen from a CD22 antigen and a CD19 antigen~~, the antigen by the cells of the lymphoma or leukemia; and

administering to the subject an antibody ~~chosen from an anti-CD22 antibody and an anti-CD19 antibody, wherein the administering the CpG oligonucleotide and the antibody results in treating the B-cell malignancy~~ specific for the upregulated antigen, in an effective amount to treat the subject.

25-33. (canceled)

34. (currently amended) A method for treating a subject having a B-cell malignancy, wherein cells of the malignancy upregulate expression of a surface antigen in response to immunostimulatory CpG oligonucleotide, the method comprising:

isolating ~~a B-cell~~ malignant B cells from a ~~subject having B-cell malignancy, wherein said B-cell malignancy is a marginal zone lymphoma or B-cell chronic lymphocytic leukemia (B-CLL);~~ the subject;

identifying a surface antigen ~~chosen from CD19, CD20, and CD22 which is not expressed or which,~~ the expression of which can be upregulated in response to immunostimulatory CpG oligonucleotide, wherein the surface antigen is expressed on the surface of the B-cell by the malignant B cells in an amount lower than that of ~~a normal B-cell, and~~ normal B cells;

administering to the subject ~~(a)~~ an immunostimulatory CpG oligonucleotide between 6 and 100 nucleotides long comprising a backbone modification and at least the formula 5' X₁X₂CGX₃X₄ 3', wherein C is unmethylated and wherein X₁, X₂, X₃, and X₄ are nucleotides, in an effective amount to upregulate expression of the surface antigen ~~on the B-cell surface, by~~ the cells; and

~~(b)~~ administering to the subject an antibody specific for the upregulated surface antigen, wherein the administering the CpG oligonucleotide and the antibody results in treating the B-cell malignancy in an amount effective to treat the subject.

35-42. (canceled)

43. (currently amended) A method for treating a subject having a B-cell malignancy resistant to antibody therapy with an antibody specific for a surface antigen, wherein cells of the malignancy upregulate expression of the surface antigen in response to immunostimulatory CpG oligonucleotide, the method comprising:

administering to a ~~subject~~ the subject ~~having a B-cell malignancy resistant to therapy with an antibody specific for a surface antigen chosen from CD19, CD20, and CD22, wherein said B-cell malignancy is a marginal zone lymphoma or B-cell chronic lymphocytic leukemia (B-CLL), an antibody specific for the surface antigen and an immunostimulatory CpG oligonucleotide between 6 and 100 nucleotides long comprising a backbone modification and at least the formula 5' X₁X₂CGX₃X₄ 3', wherein C is unmethylated and wherein X₁, X₂, X₃, and X₄~~

are nucleotides, ~~wherein the CpG oligonucleotide is administered in an effective amount to upregulate expression of the surface antigen on the B-cell malignancy, and by the cells; and~~
~~wherein the administering the antibody and the CpG oligonucleotide results in treating the B-cell malignancy~~ to the subject an antibody specific for the upregulated surface antigen, in an effective amount to treat the subject.

44-55. (canceled)

56. (currently amended) A method for treating cancer in a human, the method comprising:
administering to a human having a cancer, wherein cells of the cancer upregulate expression of a surface antigen in response to immunostimulatory CpG oligonucleotide, with ~~cells expressing a cell surface antigen~~ an immunostimulatory CpG oligonucleotide between 6 and 100 nucleotides long, said nucleic acid comprising at least the formula 5' X₁X₂CGX₃X₄ 3', wherein C is unmethylated and wherein X₁, X₂, X₃, and X₄ are nucleotides, in an effective amount to upregulate expression of the surface antigen by the cancer; and
administering to the human a human or humanized antibody of IgG1 isotype, which antibody binds to the cell surface antigen, ~~wherein the nucleic acid and the antibody are administered in an effective amount for killing the cells expressing the upregulated cell surface antigen.~~

57-77. (canceled)

78. (previously presented) The method of claim 34, wherein the surface antigen is CD19.

79. (previously presented) The method of claim 34, wherein surface antigen is CD20.

80. (previously presented) The method of claim 34, wherein surface antigen is CD22.

81. (previously presented) The method of claim 34, wherein the B-cell malignancy is B-CLL.

82. (previously presented) The method of claim 34, wherein the B-cell malignancy is marginal zone lymphoma.
83. (previously presented) The method of claim 43, wherein the surface antigen is CD19.
84. (previously presented) The method of claim 43, wherein the surface antigen is CD20.
85. (previously presented) The method of claim 84, wherein the antibody is Rituximab.
86. (currently amended) The method of claim 43, wherein the surface antigen is ~~CD20~~ CD22.
87. (new) The method of claim 43, wherein the B-cell malignancy is a marginal zone lymphoma.
88. (new) The method of claim 43, wherein the B-cell malignancy is B-cell chronic lymphocytic leukemia.
89. (new) The method of claim 43, wherein the modified backbone is a phosphate backbone modification.
90. (new) The method of claim 43, wherein the immunostimulatory CpG oligonucleotide is 8 to 40 nucleotides in length.
91. (new) The method of claim 43, wherein the immunostimulatory CpG oligonucleotide is a synthetic nucleic acid.
92. (new) The method of claim 43, wherein the immunostimulatory CpG oligonucleotide is ODN 2006 (SEQ ID NO:729).

93. (new) The method of claim 1, wherein the immunostimulatory CpG oligonucleotide is ODN 2006 (SEQ ID NO:729).
94. (new) The method of claim 24, wherein the antigen is CD19.
95. (new) The method of claim 24, wherein the antigen is CD22.
96. (new) The method of claim 24, wherein the modified backbone is a phosphate backbone modification.
97. (new) The method of claim 24, wherein the immunostimulatory CpG oligonucleotide is 8 to 40 nucleotides in length.
98. (new) The method of claim 24, wherein the immunostimulatory CpG oligonucleotide is a synthetic nucleic acid.
99. (new) The method of claim 24, wherein the immunostimulatory CpG oligonucleotide is ODN 2006 (SEQ ID NO:729).
100. (new) The method of claim 34, wherein the surface antigen is not expressed on the malignant B cells.
101. (new) The method of claim 34, wherein the modified backbone is a phosphate backbone modification.
102. (new) The method of claim 34, wherein the immunostimulatory CpG oligonucleotide is 8 to 40 nucleotides in length.

103. (new) The method of claim 34, wherein the immunostimulatory CpG oligonucleotide is a synthetic nucleic acid.

104. (new) The method of claim 34, wherein the immunostimulatory CpG oligonucleotide is ODN 2006 (SEQ ID NO:729).